SUPPORT FOR THE AMENDMENTS

Applicants have amended Claim 16 to change:

"wherein the ratio of HFA 227:HFA 134a ranges from 10:90 to 90:10 and said ratio is selected to produce ***an aerosol*** having an MMAD (mass median aerodynamic diameter) greater that 2μm, wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm;

wherein ***said aerosol has*** an MMAD greater that 2μm, and

wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm"

to

"wherein the ratio of HFA 227:HFA 134a ranges from 10:90 to 90:10 and said ratio is selected to produce ***aerosol particles*** having an MMAD (mass median aerodynamic diameter) greater that 2μm, wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm;

wherein ***said aerosol particles have*** an MMAD greater that 2μm, and

wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm."

Support for this amendment can be found on page 12, lines 26-28, of the present specification.

No new matter has been added. Claims 16-17 and 28-33 are active.

REMARKS

Present Claims 16, 17, and 28-30 relate to aerosols which are produced from a solution consisting of:

one or more solubilized active material(s),

a propellant consisting of a mixture of HFA 227 and HFA 134a, and ethanol as a cosolvent;

wherein the ratio of HFA 227:HFA 134a ranges from 10:90 to 90:10 and said ratio is selected to produce aerosol particles having an MMAD (mass median aerodynamic diameter) greater that 2μm, wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm;

wherein said aerosol particles have an MMAD greater that 2μm, and

wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm.

Present Claims 31-33 relate to aerosol inhalers which produce such an aerosol.

The inventors have discovered that the present aerosols are particularly effective for delivering substances to the respiratory tract.

The cited reference neither discloses nor suggests the presently claimed aerosols or the benefits provided thereby. Accordingly, this reference cannot affect the patentability of the present claims.

The rejection of Claims 16-17 29 and 31-33 were rejected under 35 U.S.C. 102(b) in view of U.S. Patent No. 5,653,961 (McNally et al.) and the rejection of Claims 28 and 30 under 35 U.S.C. 103(a) in view of McNally et al., and further in view of U.S. Patent No. 5,190,029 (Byron et al.) are respectfully traversed.

As explained in the present specification, the deposition of aerosol particles in the respiratory tract is affected by several factors, of which the most important are the Fine Particle Dose and the aerodynamic particle size (*see*, page 4, lines 23-26, of the present specification).

The Fine Particle Dose (FPD) gives a direct measure of the mass of particles within a specified size range, in the present case below 4.7 microns (*see*, page 5, lines 2-4 and page 16, lines 1-4, of the present specification).

On the other hand, the particles in the aerosol cloud are characterized by the mass median aerodynamic diameter (the MMAD), *i.e.* the diameter around which the mass aerodynamic diameters are distributed equally (*see*, from page 4, line 26 to page 5, line 1, of the present specification). The size distribution and the MMAD of aerosol particles for inhalation are important with respect to both efficacy and safety of the aerosolized active material(s) (*see*, page 6, lines 11-26, of the present specification).

The particle size distribution within a specific range of mass particles can vary considerably, as can be noticed also from Table 1 on page 17 of the present specification, wherein aerosols containing similar amounts of particles below 4.7 microns (col. 4) are composed of particles having an MMAD ranging from about 2.5 to about 4.0 microns.

The MMAD of the aerosol particles of the invention is not less than 2 microns (*see*, page 12, lines 26-28, of the present specification).

Thus, the aerosol claimed in claim 1 meets two requirements: it is composed of at least 40% of fine particles having a diameter of less than 4.7 microns and the MMAD of the particles is greater than 2 microns.

As already pointed out in our previously filed response, the inventors have found that by changing the ratio between the two fluorocarbon propellants it is possible to modulate and control the MMAD of the aerosol particles, to optimize the aerodynamic particle size characteristics, while simultaneously providing an aerosol having a high fraction (>40%) of fine particles.

McNally et al. is totally silent about the MMAD and the particle size distribution of its aerosol formulations.

In the Office Action, it is noted that McNally et al. discloses formulations in Examples 1-2 having a respirable fraction (*i.e.* the percent by weight of particles having an aerodynamic particle size less than 4.7 microns) ranging from 45% to 69%.

However, in this respect, it is once again respectfully submitted that McNally et al. only discloses the percent by weight of particles having an aerodynamic particle size less than 4.7 microns (ranging from 45% to 69%), but not the MMAD of the particles, whose size, as said before, can vary in a rather large range.

Furthermore, the formulations of Examples 1 and 2 of McNally et al. contain only one propellant, P134a (HFA 134a) or P227 (HFA 227), respectively. Moreover, only some of the formulations of Examples 11-50 were prepared by using a mixture of the two propellants in the 50:50 ratio, but no information are given for these formulations as far as the respirable fraction and even less the MMAD characteristics are concerned.

Applicants respectfully submit that there is nothing in Byron et al. which can cure these basic deficiencies of McNally et al. In particular, Byron et al. also does not disclose or suggest aerosols having the physical characteristics of those of the invention, nor teach how to make such aerosols.

Accordingly, the rejections should be withdrawn.

The rejection of Claims 16-17 and 28-33 under the judicially-created doctrine of obviousness-type double patenting in view of claims 1-12, 14 and 16-29 of U.S. Patent No. 6,713,047; the rejection of Claims 16-17 and 30-32 under the judicially-created doctrine of obviousness-type double patenting in view of claims 1-14 and 22-24 of U.S. Patent No. 6,964,759; and the rejection of Claims 16-17 and 28-32 under the judicially-created doctrine of obviousness-type double patenting in view of claims 11-44 of U.S. Patent No. 6,713,047 are all respectfully traversed. Applicants respectfully submit that there is nothing in any of

the claims of the cited patents which would suggest the presently claimed aerosols. Accordingly, the rejections should be withdrawn.

The provisional rejection of Claims 16 and 17 under the judicially-created doctrine of obviousness-type double patenting over Claims 1, 4-7, and 13 of copending application 10/505,679 is respectfully requested to be held in abeyance pending the identification of otherwise allowable subject matter.

Applicants respectfully submit that the present application is now in condition for allowance, and early notification to that effect is earnestly solicited.

Respectfully submitted,

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